

IN THE CLAIMS

1. (currently amended) A method for preparing a humanized or human chimeric monoclonal antibody, with high effector activity, ~~characterized in that it comprises the following comprising:~~

- a) producing and purifying monoclonal antibodies obtained from different sources selected from the group consisting of, notably from cells, plants or and non-human animals, possibly either genetically modified or transformed,
- b) measuring the fucose content and the galactose content of the glycanic structures borne by the glycosylation site of the Fc region of said antibodies, and
- c) selecting antibodies for which the fucose content/galactose content ratio is less than or equal 0.6, ~~preferentially 0.5 or 0.4.~~

2. (currently amended) The method ~~according to~~ of claim 1, ~~characterized in that wherein~~ said antibodies are produced in genetically modified cells by introducing at least one vector allowing the expression of said antibodies, said cells being eukaryotic or prokaryotic cells, ~~notably selected from the group consisting of~~ cells from mammals, insects, plants, bacteria ~~or~~ and yeasts.

3. (currently amended) The method ~~according to any of claims 1 or 2, characterized in that,~~ wherein said cells are genetically modified by introducing at least one vector allowing the expression of at least one polypeptide having a glycosyl transferase activity.

4. (currently amended) The method ~~according to~~ of claim 3, ~~characterized in that wherein~~ said glycosyl transferase activity is a galactosyl transferase activity.

5. (currently amended) The method ~~according to~~ of claim 4, ~~characterized in that~~ wherein said galactosyl transferase activity is a beta(1,4)-galactosyl transferase activity or a beta(1,3)-galactosyl transferase activity.

6. (currently amended) The method ~~according to any of the preceding claims, characterized in that~~ of claim 1, wherein said cells have an activity relating to the synthesis and/or the transport of GDP-fucose and/or to the activity of an enzyme involved in adding fucose to the oligosaccharide of the glycosylation site of the antibodies, either reduced or deleted.

7. (currently amended) The method ~~according to~~ of claim 6, characterized in that wherein the enzyme involved in the synthesis of GDP-fucose is selected from the group consisting of GMD (GDP-D-mannose 4,6-dehydratase), Fx (GDP-keto-6-deoximannose 3,5-epimerase, 4-reductase) ~~or~~ and GFPP (GDP-beta-L-fucose pyrophosphorylase).

8. (currently amended) The method ~~according to~~ of claim 6, characterized in that wherein said enzyme involved in adding fucose is a fucosyl transferase.

9. (currently amended) The method ~~according to any of the preceding claims, characterized in that~~ of claim 1, wherein, if in step b), the measured ratio is larger than 0.6, a defucosylation is performed and/or galactose residues are added to said antibody before step c).

10. (currently amended) The method ~~according to the preceding claim, characterized in that~~ of claim 9, wherein said defucosylation is performed by adding a fucosidase in the medium containing the antibody.

11. (currently amended) The method according to ~~any of claims 8 or 9, characterized in that~~ of claim 1, wherein the

addition of galactose residues is performed by adding a galactosyl transferase in the medium containing the antibody.

12. (currently amended) The method according ~~to any of the preceding claims, characterized in that~~ of claim 1, wherein said cells stem from animal or human cell lines selected from the group consisting of ~~, said lines being notably selected notably from lines of rat myelomas notably YB2/0, rat myeloma and IR983F, of human myeloma such as Namalwa, or any other cell of human origin, such as PERC6, CHO lines, notably CHO-K, CHO-Lec10, CHO-Lec1, CHO Pro-5, CHO dhfr-, CHO Lec13 lines, or other lines selected from Wil-2, Jurkat, Vero, Molt-4, COS-7, 293-HEK, BHK, K6H6, NSO, SP2/0-Ag 14 and P3X63Ag8.653.~~

13. (currently amended) The method ~~according to any of the preceding claims, characterized in that~~ of claim 1, wherein said antibody is an IgG type human immunoglobulin.

14. (currently amended) The ~~preparation~~ method ~~according to any of the preceding claims, characterized in that the~~ of claim 1, wherein said antibody is selected from the group consisting of an anti-Rhesus factor (anti-D), anti-CD, anti-tumors, anti-virus, anti-CD20-~~or~~ and anti-HLA-DR.

15. (currently amended) The method ~~according to any of the preceding claims, characterized in that~~ of claim 1, wherein said effector activity is a ADCC type functional activity.

16. (original) A method for increasing the effector activity of a composition of immunologically functional molecules, comprising the increase in galactose content and/or reduction in fucose content of the composition of molecules.

17. (currently amended) The method ~~according~~ of claim 16, ~~characterized in that~~ wherein said immunological functional molecules are monoclonal or polyclonal antibodies.

18. (currently amended) The method ~~according to any claims 16 or 17, characterized in that~~ of claim 16, wherein said molecules have high fucose content in the native condition.

19. (currently amended) The method ~~according to any claims 16 to 18, characterized in that~~ of claim 16, wherein the reduction in fucose content is due to a defucosylation of said composition through the action of a fucosidase, ~~notably an α ,1,6 fucosidase.~~

20. (currently amended) The method ~~according to any claims 16 to 19, characterized in that~~ of claim 16, wherein the increase in galactose content of said composition is due to a galactosylation of the composition through the action of a galactosyl transferase.

21. (original) A cell derived from the YB2/0 cell line, in which at least one vector coding for an antibody molecule is introduced, said cell producing an antibody for which the fucose content/galactose content ratio of the oligosaccharides of the glycosylation site of the Fc region of the antibodies is less than or equal to 0.6.

22. (currently amended) The cell ~~according to claims 21, characterized in that it~~ of claim 21, wherein said cell is transfected with an expression vector coding for a galactosyl transferase.

23. (currently amended) The cell ~~according to any of claims 21 or 22, characterized in that~~ of claim 21, wherein said galactosyl transferase is a beta(1,4)-galactosyl transferase or a beta(1,3)-galactosyl transferase.

24. (currently amended) The cell ~~according to any of claims 21 to 23, characterized in that~~ of claim 21, wherein said cell overexpresses said galactosyl transferase.

25. (currently amended) The cell ~~according to any of claims 21 to 24, characterized in that~~ of claim 21, wherein said galactosyl transferase is coded by a sequence originating from humans, mice, hamsters, cows, sheep, goats, pigs, horses, rats, monkeys, rabbits or chickens.

26. (currently amended) The cell ~~according to claim 25, characterized in that~~ of claim 25, wherein said sequence is the NM 001497, AB 024434, NM 003780, BC 053006, XM 242992, or NM 177512 sequence.

27. (currently amended) A method for preparing antibodies for which the glycanic structures borne by the glycosylation site of the Fc region has a fucose content/galactose content ratio less than or equal to 0.6, ~~preferentially less than 0.5 or even 0.4~~, comprising the culture of a cell ~~according to any of claims 21 to 26~~ in a culture medium and under conditions allowing expression of said vectors.

28. (currently amended) Therapeutic antibodies having high effector activity ~~capable of being~~ obtained from the method of claim 1, wherein ~~according to any of claims 1 to 20 and 27, said antibodies being characterized in that they~~ have on their glycosylation site of the Fc region, glycanic structures having a fucose content/galactose content ratio less than 0.6, ~~preferentially less than 0.5 or even 0.4~~.

29. (original) A pharmaceutical composition comprising an antibody according to claim 28 and at least one excipient.

30. (currently amended) A pharmaceutical composition comprising at least 50%, ~~preferentially 60%, 70%, 80% or even 90% or 99%~~ of a monoclonal antibody for which the glycanic structures borne by the glycosylation site of the Fc region have a fucose content/galactose content ratio less than 0.6, ~~preferentially less than 0.5 or even 0.4~~.

31. (currently amended) The pharmaceutical composition ~~according to any of claims 29 or 30, wherein the antibody is directed against a non-ubiquitous normal antigen, notably a Rhesus factor, such as the Rhesus factor (D) of the human red corpuscle, or an antigen of a pathological cell or on a pathogenic organism for humans, in particular against an antigen of a cancer cell.~~

32. (currently amended) The pharmaceutical composition ~~according to any of claims 29 to 31, characterized in that,~~ wherein said antibodies are IgGs.

33. (currently amended) A method for ~~The use of an antibody according to claim 28 for preparing a drug intended for treating allo-immunization, notably the hemolytic disease of the newborn child comprising administering the antibody of claim 28 to a patient in need thereof.~~

34. (currently amended) A method for ~~The use of an antibody according to claim 28 for preparing a drug intended for treating an auto-immune diseases, a cancers and or an infections by a pathogenic agents, notably for treating diseases selected from Sezary's syndrome, solid cancers, notably for which the antigenic targets are weakly expressed, notably breast cancer, pathologies related to the environment notably affecting persons exposed to polychlorinated biphenyls, infectious diseases, notably tuberculosis, chronic fatigue syndrome (CFS), parasite infections such as schistosomulas, and viral infections comprising administering the antibody of claim 28 to a patient in need thereof.~~

35. (currently amended) A method for ~~The use of an antibody according to claim 28 for preparing a drug intended for treating cancers of positive class II HLA cells, acute lymphoid leukemias of B- and T-cells, acute and chronic myeloid leukemias, Burkitt's lymphoma, Hodgkin's lymphoma, myeloid leukemias, T-cell lymphomas, and non-Hodgkinian lymphomas,~~

comprising administering the antibody of claim 28 to a patient in need thereof.

36. (currently amended) The method of claim 33, wherein
~~said~~~~The use according to any of claims 33 to 35 characterized in~~
~~that the antibody is an anti-HLA-DR or an anti-CD20.~~

37. (currently amended) A method for inducing~~The use of an~~
~~antibody according to claim 28 for manufacturing a drug intended~~
~~to induce~~ expression of IL-1 α , IL-1 β , IL-2, IL-3, IL-4, IL-5,
IL-6, IL-12, IL-18, IL-21, TGF β 1, TGF β 2, TNF α , TNF β , IFB γ , and or
IP10 by natural effector cells of the immune system, ~~said drug~~
~~being notably useful for treating cancer and viral, bacterial or~~
~~parasite infections~~ comprising administering the antibody of
claim 28 to a patient in need thereof.

38. (currently amended) A method for~~The use of an~~
~~antibody according to claim 28 for manufacturing a drug intended~~
for treating patients having one of the polymorphisms of CD16,
in particular V/F158 or F/F158, notably patients in a condition
of therapeutic failure with the presently available antibodies
or subject to undesirable secondary effects comprising
administering the antibody of claim 28 to a patient in need
thereof.

39. (currently amended) A method for preparing a human or
humanized chimeric monoclonal antibody having low effector
activity, ~~characterized in that it comprises the following~~
~~steps~~comprising:

- a) producing and purifying monoclonal antibodies obtained
from different sources, ~~notably from~~ selected from the
group consisting of cells, plants, or and non-human
animals, possibly either genetically modified or
transformed,
- b) measuring the fucose content and the galactose content
of the glycanic structures borne by the glycosylation site
of the Fc region of said antibodies,

c) selecting antibodies for which the fucose content/galactose content ratio is larger than 0.6.

40. (currently amended) The method ~~according to~~ of claim 39, ~~characterized in that~~ wherein said antibodies are produced in genetically modified cells by introducing at least one vector allowing expression of said antibodies, said cells being eukaryotic or prokaryotic cells, ~~notably selected from the group consisting of~~ cells from mammals, insects, plants, bacteria, or yeasts.

41. (currently amended) The method ~~according to any of~~ ~~claims 39 or 40, characterized in that~~ of claim 39, wherein said cells are genetically modified by introducing at least one vector allowing expression of at least one polypeptide having a glycosyl transferase activity.

42. (currently amended) The method ~~according to~~ of claim 41 ~~characterized in that~~ wherein said glycosyl transferase activity is a fucosyl transferase activity, ~~notably an α 1,6-fucosyl transferase activity.~~

43. (currently amended) The method ~~according to any of~~ ~~claims 39 to 42, characterized in that~~ of claim 39, wherein said cells have an activity relating to the synthesis and/or the transport of UDP-galactose and/or to the activity of an enzyme involved in adding galactose to the oligosaccharide of the glycosylation site of the antibodies, either reduced or deleted.

44. (currently amended) The method ~~according to~~ of claim 43, ~~characterized in that~~ wherein said enzyme involved in the addition of galactose is a galactosyl transferase, ~~notably a β 1,4-galactosyl transferase.~~

45. (currently amended) The method ~~according to any of~~ ~~claims 39 to 44, characterized in that~~ of claim 39, wherein, if in step b), the measured ratio is less than 0.6, fucosylation is

performed, and/or galactose residues are removed from said antibody before step c).

46. (currently amended) The method ~~according to~~ of claim 45, ~~characterized in that~~ wherein said degalactosylation is performed by adding a galactosidase in the medium containing the antibody.

47. (currently amended) The method ~~according to any of~~ claims 45 or 46, characterized in that of claim 45, wherein addition of fucose residues is performed by adding a fucosyl transferase in the medium containing the antibody.

48. (currently amended) The method ~~according to any of~~ claims 39 to 47, characterized in that of claim 39, wherein said antibody is an IgG type human immunoglobulin.

49. (currently amended) The ~~preparation method according to any of claims 39 to 48, characterized in that the~~ of claim 39, wherein said antibody is directed against a CD, a differentiation marker of human blood cells or against a pathogenic agent or its toxins, listed as being particularly dangerous in the case of bioterrorism, selected from the group consisting of ~~notably~~ *Bacillus anthracis*, *Clostridium botulium*, *Yersinia pestis*, *Variola major*, *Francisella tularensis*, filoviruses, arenaviruses, *Brucella species*, *Clostridium perfringens*, *Salmonella*, *E.coli*, *Shigella*, *Coxiella burnetti*, ricin toxin, *Rickettsia*, viral encephalitis viruses, *Vibrio cholerae* ~~or~~ and hantavirus.

50. (currently amended) The method ~~according to claims 39 to 49, characterized in that~~ of claim 39, wherein said effector activity is an ADCC type functional activity.

51. (original) A method for reducing the activity of a composition of immunologically functional molecules, comprising

the increase in the fucose content and/or the reduction in the galactose content of said composition.

52. (currently amended) The method ~~according to~~ of claim 51, ~~characterized in that~~ wherein said immunologically functional molecules are monoclonal or polyclonal antibodies.

53. (currently amended) The method ~~according to any of claims 51 or 52, characterized in that~~ of claim 51, wherein the increase in the fucose content is due to fucosylation of said composition through the action of a fucosyl transferase.

54. (currently amended) The method ~~according to any of claims 51 to 53, characterized in that~~ of claim 51, wherein the reduction in the galactose content of said composition is due to degalactosylation of the composition through the action of a galactosidase.

55. (currently amended) An antibody ~~composition capable of being obtained from a method of claim 39 according to any of claims 39 to 54.~~

56. (currently amended) A method ~~The use of the composition according to claim 55 for preparing a drug intended for treating and/or preventing auto-immune diseases, allo-immunizations, notably PTI, graft rejection, allergies, asthma, dermatites, urticarias, erythemas, or inflammatory diseases comprising administering the antibody of claim 55 to a patient in need thereof.~~

57. (original) A method for controlling the activity of a composition of immunologically functional molecules, comprising the regulation of the fucose content/galactose content ratio of the oligosaccharides of the glycosylation site of the Fc region of the antibodies.